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EXAMINER
MEHTA, ASHWIN D

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/892,635	MAY ET AL.
	Examiner	Art Unit
	Ashwin Mehta	1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 27 August 2004.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 17-44 is/are pending in the application.
 4a) Of the above claim(s) 32 and 33 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 17-31 and 34-44 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 28 June 2001 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>6282001</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 17-31 and 34-44, in the reply filed on August 27, 2004 is acknowledged. The traversal is on the ground(s) that Applicants believe that the protein of Group II is encoded by the DNA of Group I, that the search for the claims of Groups I and II would therefore necessarily overlap, and as a result it would not be an undue burden to examine both groups together (response, paragraph bridging pages 1-2). This is not found persuasive because the protein of Group II may be any protein, as long as it is not encoded by coding sequence naturally operably linked to the banana DNA regulatory element of the chimeric gene of claim 21. The invention of Group I is drawn to an isolated and purified banana DNA regulatory element and a method for expression of a heterologous protein in fruit, comprising using the regulatory element to control transcription of any heterologous coding sequence. A search for any and all heterologous proteins would not reveal any information at all concerning the regulatory element. As the protein of Group II does not have anything to do with the operability of the regulatory element of Group I, it would be an undue burden to additionally search and examine the invention of Group II.

The requirement is still deemed proper and is therefore made FINAL. Claims 17-31 and 34-44 are examined in this Office action. Non-elected claims 32 and 33 are withdrawn from consideration and require cancellation.

Specification

2. The specification fails to comply with the sequence rules of 37 CFR 1.821-1.825. A nucleotide sequences is recited on page 34, line 2 of paragraph [0091], and page 38, lines 10, 11, and 13 of paragraph [0097], which must be referenced by their sequence identifiers.
3. The brief description of Figure 17 indicates that one of the sequences in the figure is SEQ ID NO: 27, and that the figure displays “Chitinase DNA and amino acid sequence.” However, it is unclear that the nucleotide sequence in Figure 17 is a chitinase DNA encoding a chitinase amino acid sequence. SEQ ID NOs: 44 and 45 have rather high sequence identity, 98% and 97%, with SEQ ID NO: 27 and, as discussed below, the specification indicates that SEQ ID NOs: 44 and 45 are the putative promoter of the banana p31 gene. Applicants are asked to review the sequences in the sequence listing and that they are referred to correctly in the specification. Correction/clarification is required. New matter must be avoided.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 17-31 and 34-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 17 and 21: the recitation, “5’ or 3’ to a gene” renders the claims indefinite. It is not clear if the regulatory element is a part of the gene, or if it can be any regulatory element of any gene located anywhere on the same chromosome, but 5’ or 3’ to the gene.

Further in claims 17 and 21: the recitation, “a gene which is differentially expressed during fruit development” render the claims indefinite. It is not exactly clear what is meant by “differentially.” What is the nature of the differential expression? That is, is the gene expressed at reduced levels during fruit development, expressed at higher levels during fruit development, not expressed at all during fruit development, expressed at varying levels during different times of fruit development, expressed only in fruit cells during fruit development and not in other plant tissues, etc.

In claim 18: the recitation, “ethylene signal” renders the claim indefinite. It is not clear what all of the signals are that can be considered to be “ethylene signals”. What other signals, besides ethylene itself, are ethylene signals?

In claim 21: the recitation, “derived from a sequence” renders the claims indefinite. It is not clear what is meant by “derived” in the context of the claim. The metes and bounds of the claim are unclear.

In claim 25: the recitation, “plant developmental signal” renders the claims indefinite. It is not exactly clear what signals are to be considered as plant developmental signals. The metes and bounds of the claim are unclear.

In claims 39 and 42: the recitation, “a 5’ upstream promoter region” renders the claim indefinite. The article “a” suggests that there is more than one promoter region. However, genes possess only one promoter. The metes and bounds of the claim are unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 17-31 and 34-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards any isolated and purified banana DNA regulatory element which is 5' or 3' to any gene which is differentially expressed during fruit development; or wherein said element is activated by any ethylene signal; or a chimeric gene comprising a heterologous DNA molecule operably linked to any banana DNA regulatory element naturally found, or derived from a naturally found sequence, that is 5' or 3' to any differentially expressed gene during fruit development; any plant genome comprising said chimeric gene; any plant cell or plant comprising said chimeric gene; a method for expression of heterologous protein in fruit comprising transforming fruiting plants with said chimeric gene; fruit produced by said method; or said regulatory element or chimeric gene wherein said element is a 5' upstream promoter region of the p31 gene, or has the nucleotide sequence of SEQ ID NO: 44 or 45 or any fragment thereof.

The specification indicates that the 5' flanking region containing the putative promoter of the banana p31 gene is set forth in SEQ ID NO: 44 (pages 48-50). An NcoI site at position –

1741 relative to the start codon of the p31 gene was removed, and a new NcoI site was inserted that spans the translation start. The nucleotide sequence containing the new NcoI site is set forth in SEQ ID NO: 45 (pages 50-52). The p31 promoter was fused to the GUS coding sequence, inserted into an Agrobacterium binary vector and introduced into tomato. The specification indicates that GUS staining was observed primarily in vascular and placental tissue of fruit of transgenic plants, and no staining was observed in leaf, petiole, or stem tissues (pages 52-53).

However, the specification does not describe any isolated banana DNA regulatory element other than those set forth in SEQ ID NOs: 44 and 45. The structures of SEQ ID NOs: 44 and 45 do not provide any information concerning the structure of any other banana DNA regulatory element of any gene. The specification does not correlate the transcription promoting activity of SEQ ID NOs: 44 and 45 with any other structures. The specification also does not describe any fragments of SEQ ID NOs: 44 and 45 that retain their functional activity. The specification does not describe the regions of SEQ ID NOs: 44 and 45 that are essential to their fruit-specific promoter activity, and which must be in every fragment of SEQ ID NOs: 44 or 45 that retain their activity.

The specification also does not describe every plant genome that comprises the chimeric gene of claim 21. Such genomes would comprise more than a chimeric gene that comprises SEQ ID NO: 44 or 45. The specification does not describe the structures and functions of all other genes of all plant genomes broadly encompassed by the claim. Given the breadth of the claims encompassing any and all isolated banana DNA regulatory elements 5' or 3' to any gene differentially expressed in fruit, all plant genomes comprising the claimed chimeric gene, and fragments of SEQ ID NOs: 44 and 45 that retain their functional activity, and the lack of written

description as discussed above, the specification fails to provide an adequate written description of the multitude of regulatory elements and plant genomes encompassed by the claims.

5. Claims 17-31 and 34-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the promoter sequences set forth in SEQ ID NOs: 44 and 45, chimeric genes comprising SEQ ID NO: 44 or 45 operably linked to a heterologous DNA molecule, and a method for expressing a heterologous protein in fruit comprising a chimeric gene comprising SEQ ID NO: 44 or 45, does not reasonably provide enablement for any other isolated and purified banana DNA regulatory element that is 5' or 3' to a gene differentially expressed in fruit development or fragments of SEQ ID NOs: 44 and 45 that retain its functional activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn towards any isolated and purified banana DNA regulatory element which is 5' or 3' to any gene which is differentially expressed during fruit development; or wherein said element is activated by any ethylene signal; or a chimeric gene comprising a heterologous DNA molecule operably linked to any banana DNA regulatory element naturally found, or derived from a naturally found sequence, that is 5' or 3' to any differentially expressed gene during fruit development; any plant genome comprising said chimeric gene; any plant cell or plant comprising said chimeric gene; a method for expression of heterologous protein in fruit comprising transforming fruiting plants with said chimeric gene; fruit produced by said method; or said regulatory element or chimeric gene wherein said element is a 5' upstream promoter

region of the p31 gene, or has the nucleotide sequence of SEQ ID NO: 44 or 45 or any fragment thereof.

As discussed above, the specification indicates that the 5' flanking region containing the putative promoter of the banana p31 gene is set forth in SEQ ID NO: 44 (pages 48-50). An NcoI site at position -1741 relative to the start codon of the p31 gene was removed, and a new NcoI site was inserted that spans the translation start. The nucleotide sequence containing the new NcoI site is set forth in SEQ ID NO: 45 (pages 50-52). The p31 promoter was fused to the GUS coding sequence, inserted into an Agrobacterium binary vector and introduced into tomato. The specification indicates that GUS staining was observed primarily in vascular and placental tissue of fruit of transgenic plants, and no staining was observed in leaf, petiole, or stem tissues (pages 52-53).

However, the specification does not teach any isolated and purified banana DNA regulatory elements other than those set forth in SEQ ID NOs: 44 and 45, or fragments of SEQ ID NOs: 44 and 45 that retain their functional activity. No guidance is provided at all concerning the regions within SEQ ID NOs: 44 and 45 that are essential to their functional activity. One skilled in the art cannot predict what subsequences of SEQ ID NOs: 44 and 45 would retain functional activity. In the absence of further guidance, one skilled in the art is left to make all possible fragments of all possible sizes and test them for retention of activity, which amounts to undue experimentation. Given that SEQ ID NOs: 44 and 45 are 2156 and 2160 bases, respectively, this is not a trivial matter. See Genentech, Inc. v. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention. Given the breadth of the

claims encompassing any and all isolated banana DNA regulatory elements 5' or 3' to any gene differentially expressed in fruit, all plant genomes comprising the claimed chimeric gene, and fragments of SEQ ID NOS: 44 and 45 that retain their functional activity, unpredictability of the art and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 17-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Lopez-Gomez et al. (Plant Science, March 1997, Vol. 123, pages 123-131).

The claims are broadly drawn towards any isolated and purified banana DNA regulatory element which is 5' or 3' to any gene which is differentially expressed during fruit development; or wherein said element is activated by any ethylene signal, or wherein the ethylene signal is produced by developing fruit or by exogenous ethylene gas.

Lopez-Gomez et al. teach the isolated 5' flanking sequence, including the promoter region, of the banana ACC oxidase gene. The 3' untranslated region of the gene is also taught. RNA blot analysis shows that the ACC oxidase message is not detectable in preclimacteric fruit not treated with ethylene, but is observed in climacteric fruit. Ethylene production increases in ripening fruit. Message is also seen in peel and pulp in climacteric fruit, but is at higher levels in

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pulp of ethylene treated banana fruit. Expression of ACC oxidase is induced by ethylene (pages 125-129). All of the claim limitations are taught by the reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 17-31 and 34-38 rejected under 35 U.S.C. 103(a) as being unpatentable over May et al. (Bio/Technology, 1995, Vol. 13, pages 486-92) in combination with Lopez-Gomez et al. (Plant Science, March 1997, Vol. 123, pages 123-131), Mason et al. (Trends in Biotech., 1995, vol. 13, pages 388-392), and Sukhapinda et al. (Mol. Gen. Genet., 1987, Vol. 206, pages 491-497).

The claims are broadly drawn towards any isolated and purified banana DNA regulatory element which is 5' or 3' to any gene which is differentially expressed during fruit development; or wherein said element is activated by any ethylene signal; or a chimeric gene comprising a heterologous DNA molecule operably linked to any banana DNA regulatory element naturally found, or derived from a naturally found sequence, that is 5' or 3' to any differentially expressed gene during fruit development; any plant genome comprising said chimeric gene; any plant cell or plant comprising said chimeric gene; a method for expression of heterologous protein in fruit comprising transforming fruiting plants with said chimeric gene; fruit produced by said method

May et al. teach a method to stably transform banana plants and assert that banana fruits are the fourth most important food in the developing world (pages 486-490).

May et al. do not teach an isolated banana DNA regulatory element, DNA sequences encoding therapeutic proteins, or tomato plants.

Lopez-Gomez et al. teach the promoter of the banana ACC oxidase gene, as discussed above.

Mason et al. teach the use and advantages of transgenic plants to express foreign proteins, including oral vaccines, assert that vaccine production in transgenic plants addresses a need for the production and delivery of inexpensive vaccines in the developing world, and that large amounts of antigen could be produced at relatively low cost (pages 388-391).

Sukhapinda et al. teach a method to produce stably transformed tomato plants (pages 493-495).

It would have been obvious and within the scope of one of ordinary skill in the art at the time the invention was made to modify the method of transforming banana plants of May et al. by using other promoters, including that of Lopez-Gomez et al., to express desired proteins in banana fruit, such as the foreign antigens and vaccines of Mason et al. One would have been motivated to express these proteins in plants, given the need discussed by Mason et al. One would have been motivated to express the proteins in banana fruits, given that they are one of the most important foods in the developing world, as asserted by May et al. It would also have been obvious to one of ordinary skill in the art to express the proteins in fruits of other plants, such as tomato using the transformation method of Sukhapinda et al. One would have been motivated to

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introduce the ACC oxidase promoter/heterologous gene cassette into tomato, given that this is also a crop plant having worldwide economic importance.

8. Claims 17-31 and 34-44 are rejected, and non-elected claims 32-33 are withdrawn from consideration.

Contact Information

Any inquiry concerning this or earlier communications from the Examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The Examiner can normally be reached from 8:00 A.M to 5:30 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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October 15, 2004